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Little progress has been made on methods to prevent the physiologic decay experienced by flight crews during long-duration missions in space. The basic reason for this loss of physiologic adaptation is the absence of gravitational stimulation. Physiologists have attempted to prevent these physiologic alterations through diet, drugs, exercise and lower body negative pressure. Acceleration-based research programs, developing methods to counteract the effects of weightlessness in humans with centrifugation, have essentially been ignored for these last three decades. NASA has plans to put a human-use centrifuge in its Space Station. A human-use centrifuge has tremendous potential as a "cure-all" for the physiologic woes of space, its design (particularly radius, maximum G, G-onset rates, and G-duration capabilities) must be carefully considered, and based on sound physiologic knowledge that, for the most part, does not yet exist. Ground-based studies should be conducted to provide a better understanding of the human physiological consequences of centrifugation, and to better define how to beneficially apply maintenance accelerations to humans.

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COMMENTARY

A Human-Use Centrifuge for Space Stations: Proposed Ground-Based Studies

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IN WASHINGTON, DC, I recently attended the Space Life Sciences Symposium: Three Decades of Life Science Research in Space (sponsored by NASA), where the visions of long-duration missions to other planets and solar systems, as well as extended periods of weightlessness in Space Station, remain alive and well. However, it became clear, as the meeting progressed, that little progress had been made on methods to prevent the physiologic decay that accompanies long-duration stays in such a space environment. Of course, little doubt can exist that the basic reason for this loss of physiologic adaptation is the absence of gravitational stimulation. The requirement for gravity to maintain "normal" physiologic activity should not be surprising, since all animal and plant organisms have evolved in the presence of gravity.

Interestingly, and for less than obvious reasons, physiologists have attempted to prevent these physiologic alterations in space by using methods with non-accelerative bases. Specifically, these approaches have used diet, drugs, exercise, and lower body negative pressure, but without developing effective countermeasures. In retrospect, using methods that simply treat the symptoms of physiologic deconditioning is an approach that superficially is attractive, but, because the gravitation effect is ignored, should be expected to meet with some degree of failure.

At the 1987 meeting of the International Union of Physiological Sciences (IUPS)—the Commission on Gravitational Physiology—it was reported that only severe exercise regimes were effective in preventing physiological deconditioning of Cosmonauts in very long duration spaceflight. However, it was concluded that the time required for such a program and adverse effects (pain) made it unsuitable as a countermeasure for long-term spaceflight, and undoubtedly some form of artificial gravity will be required for such missions (12).

Physiologic and metabolic functions that have developed in the presence of acceleration (gravity) probably have it as an integral function in the physiologic equation. As scientists, we all know that you can "fool Mother Nature," but these past studies show that "Mother Nature is no fool!" Therefore, I was somewhat surprised to learn at the Space Life Sciences Symposium that acceleration-based research programs, developing methods to counteract the effects of weightlessness in humans with centrifugation, have essentially been ignored for these last three decades.

The Problem

Several physiologic problems develop during long durations in space; and, although these problems may be bothersome and at times serious, experts in mission planning (e.g., 2- to 3-year round trip to Mars) do not expect them to threaten mission completion (10). Interestingly, and somewhat contradictorily, there appears to be some concern within NASA that the physiologic limit for a stay in space is about 6 months.

Several physiologic alterations are commonly discussed, and have been the focus of numerous research studies primarily designed to either monitor or prevent their occurrence in space: (a) fluid shift, and decreased plasma volume; (b) orthostatic intolerance; (c) reduced tolerance to increased $+G_z$; (d) negative calcium balance, resulting in loss of bone; (e) possible immunosuppression; and (f) muscle atrophy of specific antigravity muscles (6). Aside, possibly, from the first and last physiologic effect, no known treatment except gravity or acceleration will prevent these occurrences—a

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situation that will, for the most part, continue indefinitely.

If these physiologic conditions are in fact not mission-threatening, why would anyone be concerned with their occurrences? First, I suspect that a fracture of an arm bone, during a strength-demanding activity in space, might present a mission-completion problem, particularly during a critical phase of that mission. Significant strain can occur in bones in people in space (you don't have to be at 1 G), either by twisting, turning, or pulling motions used to defeat something like a stubborn bolt or, of even greater concern, a stuck lever that might be controlling an important station or spacecraft function.

Second, space should be an environment that human beings can enter, remain in for long durations, and leave without becoming physiologic cripples—even if these severe handicaps are reversible. In that regard, some animal studies suggest that severe bone loss from simulated weightlessness may *not* be completely reversible (11).

Let's Discuss Centrifuges

Centrifuges provide acceleration fields that are indistinguishable from those provided by gravity, as postulated by Einstein's Principle of Equivalence (19). Therefore, we can provide significant "artificial gravity" where significant gravitational effects do not exist. Of course, a centrifuge in space is not a novel idea; and NASA has plans to put a human-use centrifuge in its Space Station (sometime), probably with an approximate 2-m radius. But, exactly what physiologic answers will that centrifuge, or any centrifuge in space (except for a rotating space station, which will not be available in the near future), give the scientific community? As someone who has an acute understanding of the human physiologic consequence of centrifugation, I believe that insufficient scientific knowledge is available at this time to allow someone to intelligently support or, for that matter, oppose a human-use centrifuge in space of any dimensions, much less one of 2-m radius. I have reached this conclusion even though I have a "gut feeling" that a centrifuge as a countermeasure in Space Station would be a marvelous piece of equipment that would probably solve most, if not all, of the physiologic problems of prolonged spaceflight. We already know from animal studies that long-duration increased G exposure selectively enhances peripheral vasocontractibility and baroreceptor function—phenomena that are prominent in the physiologic deconditioning process of space (7).

Because a human-use centrifuge has tremendous potential as a "cure-all" for the physiologic woes of space, its design (particularly radius, maximum G, G-onset rates, and G-duration capabilities) must be carefully considered, and based on sound physiologic knowledge that, for the most part, does not yet exist.

There is an axiom regarding human-use centrifuges that, for increased uniformity of the acceleration field—usually an important consideration—the longer the centrifuge radius, the better. This G-field uniformity is an important consideration regarding research, however the space centrifuge for human-use would be used for applied purposes. For the applied uses expected of a centrifuge in space, G-field uniformity will probably not be nearly as important; but instead, and for practical reasons, radius length will primarily depend upon the shortest radius possible to develop the G necessary to perform its function. If these functions can be afforded by an extremely short-arm radius (e.g., 5 ft, or even shorter), its use on long-duration missions (such as to Mars), where it would be potentially of great benefit (although space aboard such a vehicle would be extremely limited) might be reasonable.

The minimum radius necessary will be limited by the G gradient (head-to-foot) that will provide the G environment inside the body to support the physiologic requirements (e.g., for $+G_z$ and orthostatic tolerance determinations and maintenance, a significant vascular hydrostatic pressure between the head and heart must develop during G exposures). The scientific basis for the G gradient necessary to maintain a positive calcium balance is not known at this time, but the minimum acceleration level has been hypothesized to be at least 1 G (6).

Human tolerance to short-arm centrifuges is remarkably high. A 4.76-ft radius centrifuge that provided 100% G gradient across the human body (the head at the axis of rotation) was tolerated for 2 h without any ill effects; and rotational rates of 66 rpm for a mean of 2 min 41 s, in a group of 5 subjects, was found not to be a problem (14)—so there is no apparent human tolerance limit to the minimum-length radius centrifuge.

The physiologic responses to short radius centrifugation as they relate to the physiologic problems in space should be determined as soon as possible. Of course, these studies can be conducted on Earth. One such study, concerning orthostatic and $+G_z$ tolerance determinations, is now in progress in our laboratory (1,2). This size centrifuge was shown to be effective in control of fluid volumes (15).

A centrifuge in space has an operational difference from a rotating space station providing 1 G; namely, provision of many levels of G. This difference may make the centrifuge in space a very potent tool, but establishing suitable equipment and procedures will require considerable ground-based studies. Before we examine the possibilities of a beneficial interaction between G level and exposure time in preventing detrimental space-induced physiologic alterations, the reader should be afforded some understanding of human tolerance to G levels above 1 G for sustained periods of time.

Although, at present, the effect of G-exposure duration (of any level, for limited periods of time) upon physiologic homeostasis in humans is not known, continuous exposure to 1 G to maintain this homeostasis does not appear to be required. For instance, no more than 4 h of exposure to 1 G, with exercise, is required each day to maintain a positive calcium balance in a bed-rest study that without this 1-G exposure caused a significant negative calcium balance and bone loss (16).

Animal experiments have also demonstrated that periodic exposures to an accelerative field produce adaptive changes useful in tolerating that field continuously (3). Similar short-duration exposures could be expected to provide effective countermeasures to general physiologic deconditioning in space.

Although less than continuous G exposures appear to be necessary in space as a homeostatic tool, G exposure of several minutes to possibly even several hours may be required. Unfortunately, very little understanding exists concerning human tolerance to prolonged exposures to increased G (levels >1 G); but enough is known to realize that increased G for sufficient duration to provide a coun-

termeasure is probably well tolerated up to 3 G. A man survived exposure to 2 G for 24 h without apparent immediate adverse symptoms, although some "anesthesia sensation" in the left hand required over 2 months to resolve (5). He also exhibited a positive fluid balance (i.e., 2250-cc fluid intake with 890-cc output), and his white blood cell count doubled. However, this study shows that man is quite tolerant to G levels above normal gravity for exceedingly long periods of time. Similarly, the North American Rockwell Rotational Test Facility study found 1.6 G to be well tolerated by four subjects for several days (6). Seven subjects tolerated 3 G for 1 h without incident and 3.5 G for 30 min. However, fields above 3 G tend to be limited in duration by benign symptoms of blackout, loss of consciousness, or fatigue, so that these higher G levels would probably not be useful (13).

Let's Fool Mother Nature

Why should we be concerned with or interested in exposures greater than 1 G in a centrifuge in space? Because, for many of the physiologic parameters, the necessary G requirement may have a time-intensity summation effect that offers, in space, centrifuge exposures of "high" G for extremely short duration (possibly less than 1 h over a 24-h period of time) that are adequate for physiologic protection. The advantage, of course, is that less "unproductive" (wasted) time would be required of astronauts on the centrifuge to maintain their acceleration tolerance to Earth's gravitation effects.

On the other hand, if we found that several hours of increased G exposure was required, crewmembers could sleep on the centrifuge. Several subjects, bored by the long duration G exposure (up to 3 G) slept for various periods of time on the 4.76 ft radius centrifuge (14). Interestingly, cosmonauts have been reported to have severe and continuing sleep problems during long-term space flight (17). Possibly, centrifugation during sleep could correct this problem.

A continuous G-level and duration effect (sometimes referred to as the "Bodenheimer's Time-intensity Summation Principle") has been shown to exist, over a wide range of G levels for both animal and human G tolerances and physiologic functions, that results in the following relationship (13,18): $G \times S = K$, in which G = G level; S = G duration of exposure in seconds; and K = Constant.

In a similar type of response, erythrocyte hydration effects in primates required 60 s at 3 G, whereas at 6.5 G only 40 s of acceleration exposure was needed (9). The cardiovascular system responds (stimulation) in a like manner with a greater heart rate (more rapid stimulation) at 3 G (110 bpm) than at 1 G (70 bpm) (4).

If this G-level-duration coupling exists for calcium balance, "protective" centrifugation involving short duration exposures at some G levels above 1 G could be used in space; e.g., 3 G on a 5-ft radius centrifuge for possibly 30 min each day could be the prophylactic G exposure required to protect the Space Station crew against calcium loss in the bone.

This concept for both G tolerance and calcium metabolism can be validated with ground-based studies using several groups of bed-rest subjects, with each group receiving a different daily centrifuge exposure of a specific G-level duration, using a regular long-arm (20-ft radius) centrifuge. Upon determining the minimum G duration required to prevent bone loss during bed rest, similar exposures can be conducted to determine the minimum length radius centrifuge that provides this same protective environment. G-tolerance and orthostatic-tolerance studies can be conducted in a similar manner, and possibly in conjunction with the calcium-balance study, using the same subjects. Of course, in this instance, a G-tolerance determination control group would have to be maintained over the course of the study.

Undoubtedly, a minimum duration of recurring 1-G exposures is required to preserve each normal acceleration-influenced physiologic function. Probably, the required duration of exposure decreases with increasing G-exposure levels to achieve the same physiologic effect.

Ground-based studies should be conducted to understand this relationship and to define the minimum radius required to beneficially apply maintenance accelerations to humans. Simply putting a 2-m centrifuge into a Space Station, without previously establishing its requirements and potential for physiologic application, would be less than desirable and, indeed, difficult to support. On the other hand, once the full potential of physiologic benefits to the space inhabitant is known and useful acceleration schedules are developed on Earth, advocacy for including such a centrifuge in Space Station would be an easy matter. These studies will require considerable resources and time, but should be completed before a human-use centrifuge can be procured for Space Station.

The human centrifuge has been used for over 50 years as an enormously important research tool for delving into the mysteries of the acceleration environment. It is time that we develop an applied use for this valuable tool and let it support the human in space. But, as in any developmental process, applied uses will have to be determined, so we had better get started!

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